

WHAT IS CLAIMED IS:

1. An isolated nucleic acid encoding a protein comprising the amino acid sequence of SEQ ID NO:2 or 8 or a functional fragment thereof.

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2. The isolated nucleic acid of claim 1, wherein the protein has a cytidine deaminase activity.

10 3. An isolated nucleic acid or a fragment thereof comprising the nucleotide sequence of SEQ ID NO:1 or 7.

4. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:

15 (a) nucleotides 93 to 689 of SEQ ID NO:1; and

(b) nucleotides 80 to 676 of SEQ ID NO:7.

20 5. An isolated nucleic acid selected from the group consisting of:

(a) a nucleic acid that (i) hybridizes under stringent conditions to the nucleotide sequence of SEQ ID NO:1, and (ii) encodes a polypeptide having a cytidine deaminase activity;

(b) a nucleic acid that (i) hybridizes under stringent conditions to the nucleotide sequence of SEQ ID NO:7, and (ii) encodes a polypeptide having a cytidine deaminase activity; and

(c) a fragment of (a) or (b).

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6. A substantially pure polypeptide comprising the amino acid sequence of SEQ ID NO:2 or 8 or a fragment thereof that (a) has a cytidine deaminase activity or (b) is immunogenic.

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7. A substantially pure polypeptide comprising substantially the same amino acid sequence as that of SEQ ID NO:2 or 8 and having a cytidine deaminase activity.

8. A substantially pure polypeptide selected from the group consisting of:
(a) a mammalian polypeptide encoded by a nucleic acid that hybridizes under high stringency conditions to the sequence of SEQ ID NO:1, wherein the polypeptide has a cytidine deaminase activity; and

5 (b) a mammalian polypeptide encoded by a nucleic acid that hybridizes under high stringency conditions to the sequence of SEQ ID NO:7, wherein the polypeptide has a cytidine deaminase activity.

9. An expression vector comprising the nucleic acid of claim 1.

10 10. An expression vector comprising the nucleic acid of claim 2.

11. An expression vector comprising the nucleic acid of claim 3.

15 12. An expression vector comprising the nucleic acid of claim 4.

13. An expression vector comprising the nucleic acid of claim 5.

14. A cultured host cell comprising the expression vector of claim 9.

20 15. A cultured host cell comprising the expression vector of claim 10.

16. A cultured host cell comprising the expression vector of claim 11.

25 17. A cultured host cell comprising the expression vector of claim 12.

18. A cultured host cell comprising the expression vector of claim 13.

19. An antibody or a reactive portion thereof to the polypeptide of claim 6.

30 20. An antibody or a reactive portion thereof to the polypeptide of claim 7.



21. An antibody or a portion thereof reactive to the polypeptide of claim 8.
22. The antibody of claim 21, wherein the antibody is a monoclonal antibody.
- 5 23. A pharmaceutical composition comprising the antibody or the portion thereof of claim 21 and a pharmaceutically acceptable carrier.
- 10 24. A pharmaceutical composition comprising the antibody or the portion thereof of claim 22 and a pharmaceutically acceptable carrier.
- 15 25. A cell producing a monoclonal antibody reactive to the polypeptide of claim 6.
26. A cell producing a monoclonal antibody reactive to the polypeptide of claim 7.
- 20 27. A cell producing a monoclonal antibody reactive to the polypeptide of claim 8.
28. The cell of claim 25, wherein the cell is a hybridoma obtained by fusing, with a mammalian myeloma cell, a non-human mammalian B cell that produces a monoclonal antibody.
- 25 29. The cell of claim 26, wherein the cell is a hybridoma obtained by fusing, with a mammalian myeloma cell, a non-human mammalian B cell that produces a monoclonal antibody.
- 30 30. The cell of claim 27, wherein the cell is a hybridoma obtained by fusing, with a mammalian myeloma cell, a non-human mammalian B cell that produces a monoclonal antibody.

31. The cell of claim 25, wherein the cell is a transgenic cell transformed by introducing, into the cell, either or both of a nucleic acid encoding a heavy chain of the monoclonal antibody and a nucleic acid encoding a light chain of the monoclonal antibody.

5 32. The cell of claim 26, wherein the cell is a transgenic cell transformed by introducing, into the cell, either or both of a nucleic acid encoding a heavy chain of the monoclonal antibody and a nucleic acid encoding a light chain of the monoclonal antibody.

10 33. The cell of claim 27, wherein the cell is a transgenic cell transformed by introducing, into the cell, either or both of a nucleic acid encoding a heavy chain of the monoclonal antibody and a nucleic acid encoding a light chain of the monoclonal antibody.

15 34. An isolated nucleic acid comprising the nucleotide sequence of (a) SEQ ID NO:9, (b) SEQ ID NO:10, or (c) SEQ ID NO:35.

35. An isolated nucleic acid comprising the nucleotide sequence of (a) SEQ ID NO:11, (b) SEQ ID NO:12, (c) SEQ ID NO:13, (d) SEQ ID NO:14, or (e) SEQ ID NO:15.

20 36. An isolated nucleic acid comprising a sequence complementary to any one of:
(a) SEQ ID NO:9,
(b) SEQ ID NO:10,
(c) SEQ ID NO:11,
(d) SEQ ID NO:12,
(e) SEQ ID NO:13,
25 (f) SEQ ID NO:14,
(g) SEQ ID NO:15, or
(h) SEQ ID NO:35.

37. An isolated oligonucleotide comprising a sequence complementary to a fragment of any one of:

- (a) SEQ ID NO:9,
- (b) SEQ ID NO:10,
- 5 (c) SEQ ID NO:11,
- (d) SEQ ID NO:12,
- (e) SEQ ID NO:13,
- (f) SEQ ID NO:14,
- (g) SEQ ID NO:15, or
- 10 (h) SEQ ID NO:35.

38. The nucleic acid of claim 37, wherein the primer comprises a nucleotide sequence of any one of:

- (a) SEQ ID NO:18,
- (b) SEQ ID NO:19,
- 15 (c) SEQ ID NO:20,
- (d) SEQ ID NO:21,
- (e) SEQ ID NO:22,
- (f) SEQ ID NO:23,
- 20 (g) SEQ ID NO:24,
- (h) SEQ ID NO:25,
- (i) SEQ ID NO:26,
- (j) SEQ ID NO:27,
- (k) SEQ ID NO:28,
- 25 (l) SEQ ID NO:29,
- (m) SEQ ID NO:30,
- (n) SEQ ID NO:31,
- (o) SEQ ID NO:32,
- (p) SEQ ID NO:33, or
- 30 (q) SEQ ID NO:34.

39. A pair of isolated oligonucleotide primers selected from the group consisting of:

(a) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:31 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:32,

5 (b) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:20 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:22,

(c) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:21 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:30,

10 (d) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:24 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:25,

(e) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:23 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:27,

15 (f) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:23 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:28,

(g) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:23 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:29,

(h) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:26 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:27,

20 (i) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:26 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:28,

(j) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:26 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:29,

(k) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:34 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:28,

25 (l) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:34 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:29,

(m) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:33 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:29, or

(n) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:18 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:19.

40. A method for identifying a substance that regulates transcription of a gene encoding an AID protein comprising the amino acid sequence of SEQ ID NO:2 or 8 into mRNA, or production of the AID protein, the method comprising the steps of:

- (a) culturing, separately in the presence and the absence of the substance, 5 cells producing the AID protein, and
 - (b) (i) comparing the level of the AID protein produced by the cells cultured in the presence of the substance with the level of the AID protein produced by the cells cultured in the absence of the substance, or
 - (ii) comparing the level of the AID protein-encoding mRNA 10 transcribed in the cells cultured in the presence of the substance with the level of the AID protein-encoding mRNA transcribed in the cells cultured in the absence of the substance.

41. A method for identifying a substance that regulates transcription of a gene encoding an AID protein comprising the amino acid sequence of SEQ ID NO:2 or 8 into mRNA, or production of the AID protein, the method comprising the steps of:

- (a) culturing, separately in the presence and the absence of the substance, cells producing the AID protein and a second protein other than the AID protein, wherein transcription of a gene encoding the second protein into mRNA is dependent in the cells on the degree of transcription of the gene encoding the AID protein into mRNA, and
 - (b) comparing the level of the second protein produced by the cells 20 cultured in the presence of the substance with the level of the second protein produced by the cells cultured in the absence of the substance.

42. The method of claim 40, wherein the cells are transgenic cells transformed 25 with a gene encoding the AID protein.

43. The method of claim 41, wherein the cells are transgenic cells transformed with a gene encoding the AID protein.

30 44. The method of claim 41, wherein the cells are transgenic cells transformed with a gene encoding the AID protein and a gene encoding the second protein.

45. The method of claim 41, wherein the second protein is a reporter protein.

46. The method of claim 45, wherein comparison of the level of the second protein is comparison of the level of a signal generated by the reporter protein.

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47. The method of claim 45, wherein the reporter protein is luciferase.

48. A method for identifying a substance that inhibits an enzyme activity of an AID protein comprising the amino acid sequence of SEQ ID NO:2 or 8, the method comprising the step of:

(a) culturing, separately in the presence and the absence of the substance, mammal-derived B cells or tissues comprising the B cells, and comparing enzyme activities of the AID proteins in the B cells separately cultured, or

(b) (i) administering the substance separately to an AID gene knockout mouse whose endogenous AID gene is inactivated so that transcription of the endogenous AID gene into mRNA is inhibited, and to a normal mouse, and

(ii) comparing enzyme activities of the AID proteins in the B cells isolated from the respective mice.

20 49. The method of claim 48, wherein the enzyme activity is a cytidine deaminase activity.

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